

the conditions of the tendon reflexes and other neurological findings of the motor and sensory systems which for the most part can be determined, together with the blood and lumbar puncture findings to substantiate, from the laboratory, the clinical picture of tabes.

At this point it must be stated that patients who have a definite locomotor ataxia may, nevertheless, have a gastric or duodenal ulcer which might readily be mistaken for some form of crisis. A few years ago this picture was indelibly impressed upon my mind by a tabetic whom I had been treating for his cord disease and whom we believed to have gastric crises. His x-ray studies were entirely negative for any pathology in his gastro-intestinal tract. His symptoms were in no way relieved by any form of treatment and he very suddenly died from acute hemorrhage. At the postmortem he was found to have a very small duodenal ulcer which, although undemonstrable by the x-ray, nevertheless led to perforation and to erosion of a large vessel which resulted in his fatal hemorrhage.

#### IN CONCLUSION

In conclusion, syphilitic disease presents itself to the surgeon from many different angles. The evaluation, therefore, of the individual with syphilis, first as a surgical risk, and second, in appraisal of his syphilis as a possible cause of a surgical condition, is of vital prognostic and diagnostic importance.

Syphilis may be said, in the main, to have a casual rather than a causal relation to surgical problems. The proper appreciation of its occasional rôle as a causal factor would lead to happier end-results, less accidental infection, less unnecessary surgical intervention and a clearer concept of the devastating effect, which, through its ubiquity, syphilis may have on all other morbid processes.

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#### STATE-WIDE MENTAL HYGIENE PROGRAM: ITS IMPORTANCE TO CALIFORNIA\*

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THE need for a well-rounded-out program of mental hygiene in California has been apparent for many years.

The nation as a whole has recognized this, hence the starting of the National Committee for Mental Hygiene in this country a number of years ago.

This year Canada, our sister country on the north, will be celebrating the twentieth anniversary of the birth of the Canadian National Committee for Mental Hygiene.

In Paris, last year, was held the second International Congress on Mental Hygiene, the first having assembled in Washington, D. C., in 1930. It took the founders of this congress twenty-two years to work up such a world organization. In

1930 fifty-three foreign countries were represented, and last year a similar number were registered in Paris, indicating quite clearly that the world is awake to the necessity of mental hygiene on a broad scale.

#### CALIFORNIA'S MENTAL HYGIENE SURVEY OF NINE YEARS AGO

California did take quite a definite step nine years ago by sponsoring a mental hygiene movement. A legislative measure, appropriating \$20,000, was passed to make a survey of the situation and the importance of establishing a program, but, unfortunately, the depression immediately followed, which probably was the chief reason for the survey not being used to advantage.

This survey, headed by Dr. Frederick H. Allen of Pennsylvania, a very capable man, under the sponsorship of the State Department of Social Welfare, after an exhaustive study of approximately two years, did give some very definite and splendid recommendations, many of which will still apply at this late date. However, it is too bad to have to report that the results of this \$20,000 expenditure were put to no practical use. Conditions naturally have changed materially since that report was made, but fundamentally they are just as sound today as they were then. Therefore, it should appear to all those in California who are vitally and directly interested, and to those who should be, that we should start in where this survey ended, or on a new basis, if necessary, and develop and carry on a mental hygiene program, as such, for the best interest of the population as a whole. In fact, it is quite evident that the need of something of this kind is most essential, since so many people from other states are coming to California by the thousands each month, both because of conditions in other states and the new laws and programs for aid which have been put in effect here in the past few years. This is particularly manifested by those seeking aid from various local agencies in the communities and the early requests for admission to the various establishments within the Department of Institutions.

#### HOW CALIFORNIA IS MEETING SOME OF ITS PROBLEMS

California spends approximately \$90,000 each biennium for deporting mental patients back to their native states. If it were not for this arrangement our institutions would soon be filled with those from other states at the sacrifice of those entitled to admission by full residence requirements.

In many of the larger centers in the state and away from some of our state institutions, outpatient clinics are held, but on such a small scale that many cases are not reached until something happens to bring them to the attention of those concerned.

For many years mental hygiene clinics have been held by members of the staff of the Sonoma State Home in the twenty counties north of the Bay district. A recent survey was made covering the present fiscal year up to March 31. During this period 475 cases were examined. Of this number, 52.5 per cent ranged from low normal upward in-

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From the office of the Medical Director, Sonoma State Home, Eldridge.

tellectually, the remaining 47.5 per cent from the borderline downward, thus indicating that the majority of the so-called normal individuals needed mental hygiene advice and treatment.

Many of these should have been examined much earlier. We find many children, who, if seen in the preschool age, would undoubtedly have profited by proper advice and treatment. It is much cheaper to maintain sufficient clinics in the communities than later to have to care for individuals in our institutions, both private and state. The first few years of a child's life are the formative ones, during which period the foundation is laid for adequate social habits. If all children could have proper attention early, both physically and mentally, it would be a great factor for their future welfare.

#### NONINSTITUTIONAL PROBLEMS

No state in the country has over, approximately, 10 per cent of their mentally deficient cases in state institutions, and it is this other 90 per cent that we should be especially concerned about. If this 90 per cent can be properly and adequately reached by a properly organized program, it would be money well and economically spent.

According to a survey made a few years ago by the White House Conference on Child Health and Protection, it was indicated there were at least two per cent who fell in the mentally deficient class.

Some states have developed a control on this type of case, and in one state the law provides for identification, registration, adjudication, prevention of marriage, and supervision in the community of all the mentally defectives in the state. It consists of a central or state commission, together with a subcommission in every county in the state, operating under the control body. If some such group could be developed in our state, to cover all phases coming under the general heading of mental hygiene, it would probably meet the requirements of our needs. With this general state organization as a working body, and operated as such, or placed under the authority of an already functioning state department such as the California Department of Institutions, which now has jurisdiction over all our mental patients, it would no doubt help to keep down considerable expense.

#### CALIFORNIA DEPARTMENT OF INSTITUTIONS: ITS EXPENDITURES

The Department of Institutions is now costing approximately \$15,000,000 each biennium to operate and cares for about 26,000 cases, with an annual increase of about 800 mental cases and about 500 mental defectives. Unless some system of prevention and control is instituted, this burden will soon increase to the point that the tax burden will become so great that, instead of being able to care for more cases in our institutions, it will be just the reverse and we will revert to the old system of custodial care only. The last biennium the Department of Institutions spent \$4,000,000 on buildings alone, and at this period at least \$6,000,000 is being spent, besides a federal grant of 45 per cent of that amount. At the present rate of admissions it will require a similar amount continually to keep pace with this increase unless we do something about it.

#### THE NEXT LEGISLATURE

Since it is impossible in this brief paper to go into all phases of the necessity of a proper mental hygiene program for this big state, I wish to recommend to all interested workers in this field that steps be taken at once to revive such a movement in time for any legislative measures that might be considered necessary for the next regular session of the State Legislature.

#### HIGH POINTS IN A SUGGESTED PROGRAM

Some of the high points that would appear to be paramount in such a program are as follows:

1. Educating the public on general mental hygiene lines.
2. Suitable courses in mental hygiene be on the curriculum of certain schools and colleges in the state.
3. Identification of all mental defectives in the state.
4. Registration of all such cases in a given state department, which may or may not exist at present.
5. Supervision of all cases coming within this category.
6. The regulation of marriage in the mentally deficient, insane, and venereal disease cases.
7. Sterilization laws which will permit the operation to be done outside of institutions (bearing in mind that approximately 90 per cent of this misfit group is at large in the communities).
8. Birth control put into effect as was intended when approved by the United States Circuit Court of Appeals in November, 1936.
9. Have a special program covering the social control of the mentally deficient in the state, similar to that being done in South Dakota for the past five years.
10. Establish more special classes within the public schools or more special schools in the larger centers.
11. Establish better segregation in our state institutions for epileptics, defective delinquents, psychopaths, and psychotic children.
12. Construct a psychopathic hospital in the north and one in the south as clearing houses for all cases qualifying for such institutions, which will also give us teaching institutions for the medical colleges of the state, as has already been proposed and is being seriously considered and urged at this time.
13. That mental hygiene clinics be developed on a larger scale or in sufficient numbers to serve the state adequately.

#### IN CONCLUSION

In closing, I should like to recommend that a permanent state organization be developed at the earliest possible date to work up a detailed program to the extent that will render a decided service in every county and community within the state. Whether this organization be the official body to carry on the work afterward, or whether it be placed in one of the present state departments, like

the Department of Institutions, could be left up to the state-wide organization to decide.

It does seem, friends and coworkers, that with the great increase of mental cases each year, and the present state of our civilization, this mental field is being overlooked, and we should not postpone any longer trying to do more in the preventive field, if ever we expect to improve our race to the point where we can say our people in California surpass those of any other state or country.

Sonoma State Home.

## CLINICAL EXPERIENCES AND EXPERIMENTS WITH PROTAMIN-ZINC INSULIN: THE POTENTIAL DANGER OF HYPOGLYCEMIA\*†

By JAMES W. SHERRILL, M.D.  
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DISCUSSION by Howard F. West, M. D., Los Angeles; H. Clare Shepardson, M. D., San Francisco; F. M. Pottinger, Jr., M. D., Monrovia.

FROM the time of the discovery of insulin by Banting, clinicians have recognized the importance of a modified form of insulin which possessed more permanent and lasting qualities. With this idea in mind many experiments have been carried out, employing various retarding processes such as oil suspension, emulsion, gelatin implants, vasoconstrictor substances, etc. Although commercial insulin serves to bring about certain metabolic alterations in the diabetic individual which closely imitate the normal, these patients are still not entirely controlled from the strict physiological standpoint. In reality, with the rapid postprandial rises in blood sugar which occur in our thoroughly treated diabetic patients, we must admit that they are in an active diabetic state 25 to 50 per cent of the time, even though painstaking methods are employed.

### PROTAMIN INSULINATE

It remained for Hagedorn and Jensen at the Steno Memorial Hospital in Copenhagen to offer an insulin compound which can be repeatedly introduced into the human organism and which is so slowly absorbed from the subcutaneous tissues that it more fully imitates the continuous secretion from the normal pancreas. Protamin insulinate, which they described, was obtained by combining an acid solution of insulin with a basic solution of protamin. The protamin which they used had not previously been described, and was obtained from the sperm of the rainbow trout-salmine iridus. Other monoprotoamin and triprotoamin compounds were tried, but proved to be unsatisfactory on account of their high solubility in the subcutaneous tissues.

### ZINC ADDITION

Fisher and Scott found the protamin prepared from Pacific Cohoe salmon, spring salmon, and steelhead salmon as effective a retarding agent as

the protamin prepared from rainbow trout. They demonstrated that the addition of a small amount of zinc prolonged the hypoglycemic effect of insulin solution to which protamin had been added. Fresh mixtures of insulin and protamin were not as effective from the hypoglycemic standpoint as those to which a small amount of zinc was added, and allowed to stand for forty hours. Scott and Fisher, at the Connaught Laboratories in Toronto, have experimented extensively with spermin derived from pancreas (and a preparation from thymus glands) as a suitable retarding agent. When combined with ordinary insulin, prolonged hypoglycemic effect was produced similar in nature to protamin. That spermin is a normal constituent of the pancreas was reported by Dudley, Rosenheim and Rosenheim in 1924. They also found that spermin occurred in commercial samples of insulin prepared by the picric-acid method; likewise, that the entire amount of spermin normally present in the pancreas could be recovered from the insulin fraction. The hypoglycemic effect of spermin-insulin compounds was prolonged when zinc was added.

The metal zinc plays an important part in the hypoglycemic action of insulin. Scott and Fisher have shown that with the addition of 0.1 per cent of zinc in the form of zinc chlorid to solutions of insulin the physiological action of insulin was greatly delayed. The blood sugars remained considerably below normal for ten hours or more. Other metals, such as cobalt, potassium, and copper, are not as effective. Zinc-insulin solutions are as effective in properly metabolizing sugar as regular insulin. Maxwell and Bischoff found that by adding basic ferric chlorid to insulin the blood sugars of rabbits and rats could be suppressed to very low levels—as long as eight hours or more. About 20 milligrams of zinc per kilogram are found in the normal pancreas of the bovine, irrespective of the age. The zinc and insulin content of the pancreas of fetal calves is exceedingly greater. Cobalt and nickel are not detected in the pancreas of either. Recently, Gray reported the results of eighteen diabetic patients of various ages treated with insulin tannate solutions over periods of a few days to two weeks. He used a preparation described by Bischoff and Maxwell, which utilized the principle of precipitating protein hormones. The relative insolubility of insulin tannate in the tissues afforded delayed absorption and prolonged liberation of free insulin. Bischoff reported active insulin compounds, using more complex protein precipitants than protamin, viz., histon. Diabetes was successfully controlled when the preparation was used alone or in conjunction with regular insulin. The blood sugar lowering effect and hypoglycemic prolongation were essentially the same as the protamin insulinate controls, using the Hagedorn-Jensen preparation.

### LITERATURE ON PROTAMIN-ZINC INSULIN

Joslin and his group treated one hundred cases of diabetes with protamin insulinate up to May, 1936. He summarizes the present status of the new substance very succinctly. "With protamin

\* From the Scripps Metabolic Clinic, La Jolla.

Read before the General Medicine Section of the California Medical Association at the sixty-sixth annual session, Del Monte, May 2-6, 1937.

† References will be given in the reprints.